

CLAIMS

1.- A recombinant adenoviral vector which contains an adenoviral genome from which the open reading frames E1 and/or E3 have been deleted, but retains enough sequence to make the adenoviral vector able to replicate in vitro, said vector also contains a therapeutic gene or a DNA sequence of interest regulated by ubiquitous promoters and/or tissue-specific promoters that encodes for therapeutic proteins useful in fibrosis treatment of the fibrosis.

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2.- The recombinant adenoviral vector according to claim 1, in which the specific tissue-promoter is PEPCK.

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3.- The recombinant adenoviral vector according to claim 1, in which the therapeutic gene or the DNA sequence cloned in such adenoviral vector is selected from latent and active human metalloprotease gene MMP-8, MMP-1, MMP-2, MMP-9 and MMP-13; human urokinase Plasminogen Activator gene (uPA wild type and/or modified), gene of the truncated receptor for TGF- $\beta$  type II; and Smad 7 which

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encode for therapeutic proteins, that degrade excess of collagenic proteins deposited in the cirrhotic organs.

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4.- The recombinant adenoviral vector according to claim 3, in which the therapeutic gene is a DNA sequence selected from the gene of the Hepatocyte Growth Factor (HGF), which encodes for proteins stimulators of hepatic regeneration with the purpose to re-establish the normal functions of the liver.

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5.- The recombinant adenoviral vector according to claim 1, in which the therapeutic proteins for the treatment of fibrosis are the latent and/or active protein MMP-8, MMP-1, MMP-2, MMP-9 and MMP-13; uPA wild type and/or modified; the truncated receptor for TGF- $\beta$  type II; betaglycan; HGF and Smad 7 .

6.- The recombinant adenoviral vector according to claim 1, which contains also the delivery of therapeutic genes or DNA sequences which encode for therapeutic proteins intended for the treatment of fibrosis in cirrhotic liver.

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7.- The recombinant adenoviral vector according to claim 6, in which the delivery of the therapeutic genes is carried out in other organs with generalized fibrosis.

8.- The recombinant adenoviral vector according to claim 7, in which the tissue-specific recognition of the therapeutic genes to the organs with fibrosis, is conducted by the administration route used.

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9.- The recombinant adenoviral vector according to claim 8, in which the administration route is endovenous.

10.- The recombinant adenoviral vector according to claim 6, in which the organs with fibrosis are selected from liver, lung, heart, kidney, skin, and hypertrophic scars.

11.- The recombinant adenoviral vector according to claim 10, in which  
5 the main target organ is the liver.

12.- Recombinant adenoviral vectors according to claims 1 to 11 in which the delivery of therapeutic genes is realised through the use of viral or non viral vectors.

13.- The recombinant adenoviral vector according to claim 12, in which  
10 non viral vectors are selected from plasmids and cationic and anionic liposomes.

14.- The recombinant adenoviral vector according to claim 6, in which the efficient sending of collagenase gene MMP-8 to cirrhotic liver, can induce the degradation of collagen by means of over-expression of metalloproteases.

15.- The recombinant adenoviral vector according to claim 1,  
characterized because it is used for the treatment of the hepatic, pulmonary, renal, heart fibrosis, keloids and hypertrophic scars, and which does not induce lethal  
15 toxicity.

16.- A process to prepare recombinant adenoviral vectors through the cloning of reporter genes Lac-Z and GFP and the therapeutic gene, which encodes  
20 for therapeutic proteins for the treatment of hepatic, pulmonary, renal, and/or heart fibrosis, keloids and hypertrophic scars.

17.- The process according to claim 16 in which the therapeutic gene is selected from the human metalloprotease gene MMP-8 latent and active, MMP-1, MMP-2, MMP-9 and MMP-13; gene for human uPA wild type and/or modified; Smad  
25 7 and gene of the truncated receptor of TGF- $\beta$  type II.

18.- The process according with claim 16 in which the recombinant adenoviral vector is pAdGFP-MMP-8.

19.- A pharmaceutical composition containing a therapeutically effective  
30 amount with a regimen of unitary doses of viral particles of recombinant adenoviral vectors, according to claim 1, for the treatment of hepatic, pulmonary, renal, and heart fibrosis, keloids and hypertrophic scars, combined with a pharmaceutically compatible carrier.

35 20.- The pharmaceutical composition according to claim 19, in which the unitary dose is of about  $10^7$ - $10^{14}$  viral particles for an individual with fibrosis.

21.- The use of recombinant adenoviral vector according with claim 1, for the elaboration of a bio-medication for the treatment of hepatic, pulmonary, renal, and heart fibrosis, keloids and hypertrophic scars.

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